THE PATH TO ELIMINATING HEPATITIS C INFECTION IN THE U.S.: EXPERTS ADDRESS HIGH DRUG PRICES, PROVIDER ENGAGEMENT, AND THE PROBLEM OF STIGMA

A thesis
Presented to the faculty of the Weill
Cornell Graduate School
of Medical Sciences
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Master of Science

By
Shashi Kapadia, MD
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ABSTRACT

Background: New curative treatments for hepatitis C have the potential to alter the course of a devastating epidemic. High drug prices, however, are widely believed to contribute to restrictions on treatment access. We aimed to learn how state health agencies have responded to the challenges of treatment access for HCV

Methods: Using a key informant interview design, we interviewed 14 health officials and 4 treatment advocates in six states. States were chosen using purposive sampling based on diverse geography, population size, known HCV treatment eligibility criteria and Medicaid expansion status. Interviews were semi-structured with questions that focused on aspects of HCV treatment access. We used content analysis to analyze transcripts for dominant themes.

Results: Treatment cost was the most significant barrier to expanding access and acted by directly influencing payers to restrict access, as well as creating the impression among guideline committees and providers that HCV treatment needed to be prioritized. Treatment eligibility criteria from state Medicaid programs did not necessarily reflect the actions of managed care organizations, who could be more variable. Additional barriers to access included stigma around HCV and substance use, as well as provider availability, especially in rural areas. The political and fiscal environment within states could aid or hinder treatment access, and evolving federal health policy surrounding Medicaid evoked concern that funding for HCV treatment access could be diminished. Individuals co-infected with HIV and HCV had additional mechanisms to access treatment.

Conclusions: While treatment eligibility criteria for HCV treatment are improving, a number of other barriers remain to achieving the scale-up needed to end the epidemic. Further work to mitigate the effects of stigma and build treatment capacity will be needed. The effects of federal health policy changes on Medicaid funding may impact states' ability to respond to this epidemic.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Kapadia, Shashi

eRA COMMONS USER NAME (credential, e.g., agency login): shkapadia

POSITION TITLE: Resident in Public Health and General Preventive Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
New York University, New York, NY	AB	05/2007	Biology
UMDNJ- New Jersey Medical School, Newark, NJ	MD	05/2011	Medicine
Rutgers New Jersey Medical School, Newark, NJ	Resident	06/2014	Internal Medicine Resident
Weill Cornell Medicine, New York, NY	Fellow	present	Infectious Diseases Fellow
Weill Cornell Medicine, New York, NY	Resident	present	Public Health and General Preventive Medicine Resident
Weill Cornell Graduate School, New York, NY	MS	present	Clinical Investigation

A. Personal Statement

My long term goal is to become an independent clinician-scientist and academic health services researcher with a focus on health disparities in the care of HIV and hepatitis C in underserved populations. My training and experience thus far has provided me with excellent preparation for a research career: prior to medical school I spent time doing direct outreach to underserved populations with two nonprofit institutions. During medical school and residency I developed expertise in adult education for communities with low health literacy. During residency and fellowship I have led research demonstrating the effectiveness of single tablet regimens in treating patients, analyzing trends in institutional HIV testing practices, exploring racial disparities in HIV treatment outcomes, modeling quality-of-life outcomes in HIV pre-exposure prophylaxis, and evaluating health policy measures for expansion of hepatitis C treatment access. In addition to these projects, I have completed coursework in biostatistics, epidemiology, clinical research methods, and qualitative research, and am working towards a Masters' of Science in Clinical Investigation which I will complete in the spring of 2017.

My primary research mentor, Dr. Bruce Schackman, is a recognized expert in the field of health economics with a focus on treatment interventions for substance use, HIV, and hepatitis C. He is the director of an NIH funded center for economic evaluations in the treatment of these diseases, and he has a strong track record of mentoring junior investigators My work on this project will lead to an application for an NIH early career research award within two years. My background and training combined with strong mentorship, a renowned research institution, and an exciting and novel project

will enable me to pursue my passion for research and contribute to the fields of implementation science as well as the treatment of hepatitis C and HIV in underserved populations.

B. Positions and Honors

Positions and Employment

2005 - 2007	Intern, South Asian Health Initiative, New York, NY
2006 - 2009	Recruitment Coordinator, South Asian Marrow Association of Recruiters, New York, NY
2008 - 2008	Fellow in Health Literacy, New York City Mayor's Office of Adult Education, New York, NY
2014 -	Fellow in Infectious Diseases, Weill Cornell Medicine, New York, NY
2015 -	Resident in Public Health and General Preventive Medicine, Weill Cornell Medicine, New York, NY

Other Experience and Professional Memberships

2010 -	Member, Gold Humanism Honor Society
2014 -	Member, Infectious Diseases Society of America
2015 -	Member, HIVMA

Honors

2003	Honors Scholar Program, New York University College of Arts and Science
2007	Magna Cum Laude, New York University
2010	Abdol Islami Foundation Scholarship, Abdol Islami Foundationb
2013	New Jersey Medical School Golden Apple Award, New Jersey Medical School Alumni Association

C. Contribution to Science

1. I have conducted and contributed to work which evaluates health disparities in the effectiveness of antiretroviral therapy for HIV. In residency, I conducted a study to evaluate the effectiveness of single-tablet regimens for HIV treatment compared to multiple tablet-regimens in an urban, mostly African-American population with high rates of poverty, substance use, and poor insurance status. This study was conducted along with Dr Sally Hodder, an experience HIV clinical researcher. I retrospectively collected viral load outcomes of HIV-infected individuals seen at one HIV clinic in Newark, NJ, finding that patients initiated on single tablet regimens had lower rates of virologic failure than those on multiple tablet regimens. This research continues to be important as single-tablet regimens are provided at a higher cost than the anticipated price of generic multiple tablet regimens that will be available in the near future, and understanding the additional benefit of these more costly regimens in populations at high risk of poor HIV outcome will be important in guiding payers and policymakers to formulate treatment recommendation. This project has been presented at a national conference and is being prepared for publication. I am now conducting an additional study to characterize social and demographic factors that are associated with virologic failure in HIV patients who are initiating antiretroviral therapy.

    a. Kapadia SN, Grant R, Hodder S. Virologic Response Better with Single Tablet Fixed Dose Antiretroviral Regimens Compared with Multiple Tablet regimens in an Urban Population of HIV Infected Persons. Infectious Diseases Society of America ID Week; 2013 October; San Francisco, CA, USA.

2. I have conducted research to evaluate the change in HIV testing practices at a large urban healthcare system in response to legislation that mandates HIV testing at initial healthcare encounters in New York State. Using data from the electronic health record, we analyzed HIV testing rates in individuals that were also undergoing testing for other sexually transmitted infections. We found that rates of HIV testing for these high-risk patients increased substantially following passage of New York State's legislation, but that over two thirds of patients seen in the ED setting and one third in the outpatient setting were still not being appropriately HIV tested. Understanding the health-system response to this legislation is important for two reasons: my work will allow our institution to target interventions to specifically raise HIV testing awareness in department that are shown to have low rates, and it will provide data for researchers and policymakers to understand the effect of this legislation and its potential impact on the HIV epidemic in New York. This research has been presented at a national conference and is currently being prepared for publication.

    a. Kapadia SN, Singh HK, Jones Sian, Merrick ST, Vaamonde CM. Missed Opportunities for HIV Testing at a large urban healthcare center 2010 -2015.. Infectious Diseases Society of America ID Week; 2016 October; New Orleans, LA, USA.

D. Additional Information: Research Support and/or Scholastic Performance

1. UL1 TR000457 Clinical and Translational Science Center – Weill Cornell: July 2015 – July 2017

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I would like to acknowledge my co-investigator, Dr. Carrie Down-Johnston at Weill Cornell Medicine for her contribution to this project.

I would also like to acknowledge contributions of mentors: Dr. Erika Martin at SUNY-Albany, Dr. Kristen Marks at Weill Cornell Medicine, Dr. Denis Nash at CUNY School of Public Health and my primary research mentor, Dr. Bruce Schackman.

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Introduction:

Hepatitis C virus (HCV) infection affects an estimated 5 million Americans.[1, 2] It is a leading infectious killer, and since 2007 has killed more Americans annually than HIV.[3] While the majority of HCV is concentrated in the 'baby boomer' generation,[4] recent increases in opioid use have led to emerging epidemics in younger persons who inject drugs.[5, 6] Hepatitis C has a long asymptomatic period that typically lasts many years, allowing for ongoing transmission and the development of severe liver disease. Indeed, hepatitis C is a leading cause of hospitalization due to liver disease and liver transplantation in the United States.[7, 8] Coinfection with HCV and HIV has a worse prognosis than HCV mono-infection with faster rates of liver fibrosis, in patients with poorly controlled HIV.[9]

Since 2014, new classes of medications called direct acting antivirals (DAAs) have been available as treatment for HCV. DAA regimens are highly effective, with cure rates consistently over 90%, and have largely replaced prior treatments.[10] Treatment of HCV is cost-effective from a societal perspective, preventing the morbidity and mortality associated with cirrhosis and liver transplantation.[11-17] Modeling studies have suggested that scale up of DAA treatment may prevent transmission and has the potential to end the epidemic.[18-20] The path to eliminating HCV requires improved diagnosis, linkage to care, and treatment uptake will be needed, especially for persons who inject drugs.[21]

Despite their potential for reducing the epidemic burden, HCV DAAs have also received negative attention from activists, media, and the healthcare sector for their high cost. With early prices approaching $84,000 per treatment course,[22] DAAs have been at the forefront of national dialogue on rising prescription drug costs. Anticipation

of these costs led state Medicaid programs to institute criteria limiting treatment to those with severe disease, abstinence from substance use, a subspecialist provider, and suppressed HIV viral loads.[23, 24] In 2014, the National Association of Medicaid Directors wrote to Congress requesting a federal response to HCV drug costs, citing the response to HIV/AIDS as an example.[25] In 2015, Centers for Medicare and Medicaid Services (CMS) instructed Medicaid programs to improve treatment access and lift treatment restrictions.[26] Judicial decisions in Washington State and elsewhere have also largely supported expanded treatment access.[27] The states' responses to the challenge of providing coverage for DAAs have varied, and the factors that have influenced policy change remain unknown.

To determine state level factors affecting DAA treatment expansion, we interviewed state health officials and treatment advocates with expertise in HCV treatment. Hypothesizing that the HIV/HCV coinfected individuals may have additional coverage options, we also interviewed experts in HCV treatment coverage for this subpopulation. We chose to conduct these interviews in 6 states that represent diverse policy environments.

Methods:

We conducted key informant interviews with experts in HCV treatment access in the United States from June 2016 to March 2017. Study methods and findings are reported using elements of COREQ criteria for reporting qualitative research.[28]

Research Team

The research team consisted of two physicians with experience in HCV treatment, (S.K. and C.J.) and two health policy researchers with qualitative research experience and expertise in federal and state policies for HIV treatment (E.M. and B.S.). All interviews were conducted by one investigator (S.K.). Data analysis was performed by three investigators. (S.K., C.J., E.M.) All four investigators met regularly to interpret data and discuss themes.

Participant Recruitment

We used purposeful sampling to select six states of interest based on purposeful sampling,[29] aiming for diverse geography, total population sizes, Medicaid expansion status, and published treatment eligibility criteria for HCV DAA coverage.[23, 24, 30] For each state, we identified up to three health officials with complementary expertise in how HCV treatment is publically financed. We also identified experts from treatment advocacy organizations and federal programs to gain a national perspective. Candidates were identified first using internet search, and then using recommendations from contacts in each state. Candidates who declined to interview were asked to identify other potential experts for interview. Additional states, and participants within them, were added to the study until theoretical saturation, when no new themes emerged from further data collection.[29] We approached 24 potential candidates: 18 agreed to be interviewed, 4 declined to be interviewed due to lack of expertise but provided referral to other potential candidates, and 2 declined to be interviewed and did not provide additional referrals. Table 1 displays characteristics of states and participants. Because of a desire for anonymity from respondents who were state employees, individual state names and respondent names or specific job titles are not reported.

Table 1:

	Number of interviews
States Included in Study	
State 1: Northeast region, Medicaid expansion, no severity criteria, no substance use criteria	2
State 2: West region, Medicaid expansion, lenient severity criteria (F2), no substance use criteria	2
State 3: South region, no Medicaid expansion, lenient severity criteria (F2), no substance use criteria	3
State 4: South region, no Medicaid expansion, no severity criteria, need for documented substance use abstinence.	1
State 5: Northeast region, Medicaid expansion, no severity criteria, no substance use criteria	3
State 6: Midwest region, Medicaid expansion, strict severity criteria (F3), need for documented substance use abstinence	3
Professional Role of Key informants	
Public Health Official – HCV Focus	5
Public Health Official – HIV/AIDS Focus	6
Public Health Official – Other	4
Advocacy or professional organization member	3

Data Collection

We used a semi-structured interview guide that focused on mechanisms that facilitated hepatitis C treatment, barriers to hepatitis C treatment, the contrast between treatment access for persons co-infected with HIV and HCV versus persons mono-infected with HCV, specific treatment eligibility criteria in state Medicaid programs, and expectations regarding future HCV treatment access. Interviews were conducted over the telephone by one investigator (S.K.) and lasted approximately 1 hour. Interviews were digitally recorded and transcribed for analysis using a commercial transcription service. In order to triangulate findings, we reviewed published literature on Medicaid and ADAP treatment criteria, and publicly available government documents regarding HCV treatment coverage in the selected jurisdictions. A copy of the interview guide is included in the appendix.

Data Analysis

De-identified transcripts were coded using content analysis.[31] A codebook was developed based on the first 4 transcripts and updated iteratively with each new transcript.[32] Two investigators (S.K., C.J.) coded all transcripts independently, and discrepancies in coding were resolved in in-person meetings. A subset of transcripts were independently coded by E.M. to refine codebook development. Codes were analyzed for themes during monthly in-person discussions by the research team. All data were coded in NVivo Software (QST International Pty Ltd., Version 11). Code labels and descriptions are included in the appendix.

Results:

Treatment cost triggers multiple barriers to expanding HCV treatment coverage

Every respondent identified the importance of high treatment cost as the most significant barrier to treatment. High initial costs when DAAs came onto market in 2014 spurred payers to limit access to treatment: "Cost concerns were just so overwhelming…and state Medicaid programs… had not budgeted for these drugs and were just grappling with how they could make access a reality. *[Professional organization member]*" One respondent was "surprised that our Medicaid initially resisted to [provide] comprehensive coverage for the HCV medications…of course, it was primarily cost driven. *[Health official, state 6]*" In some states, high cost for DAA treatment reduced enthusiasm within health agencies for prioritizing HCV treatment, A state Medicaid official stated that "there's so many other populations of people that are bigger than that who also need [treatment]…Can't help everybody. *[Health official, State 3]*"

The publicity around treatment cost created an early impression among clinical societies, policymakers, and providers that access to HCV therapy could be prioritized to those with severe disease, an idea that was incorporated into early iterations of national treatment guidelines and influenced the criteria that payers developed: “The national guidelines didn't really do us any favors…when they came out with that list of priorities, it was pretty much the nail on the coffin” [*Health Official, NY*]. In 2014, most state Medicaid programs had imposed eligibility criteria to restrict treatment access based on these priorities: such as requiring high disease severity, proof of abstinence from substance use, and a specialist treating provider. One respondent attributed these criteria to “rationing, because [payers] feel like they need to contain cost.” Respondents from every state indicated that criteria based on disease severity, which began by requiring advanced fibrosis in many states, are generally becoming less restrictive, but this was not universally the case for other criteria. The feeling that access needs to be limited to save cost may also affect provider willingness to treat HCV: one health official that surveyed local providers reported that: “Everybody is so distracted by what’s in the media that they don’t look at anything else…So many providers had said to us, ‘We’re so afraid to begin to start somebody on treatment because it’s so expensive.’ *[Health official, State 5]*” Even as payers are relaxing treatment eligibility criteria in order to cover treatment, providers may be informally adapting similar criteria in the office setting to determine a patient’s readiness for treatment, limiting the impact of more lenient policies.

All respondents expressed frustration about the lack of transparency in drug pricing and treatment utilization, which hampered efforts to improve access. Health officials in five states described difficulties accessing information on treatment coverage and drug prices from private payers and other governmental agencies. This lack of transparency “made it hard to hold any party accountable, and that makes it difficult for

the work of advocates or providers or patients." One respondent was "frustrated by the lack of information…the media is very quick to jump on a $1,000 a pill headline…but there's also been a lack of nuance about the fact that the wholesale acquisition cost for drugs is not actually what anybody pays. [*Treatment advocate*]" On the other hand, another respondent noted the potential benefit of some degree of secrecy: "many of the states where you have seen changes in the last year, part of the motivation for those changes has been behind the scenes negotiations with the drug companies to get more favorable rebate agreements."

Despite the strong uniform concern about the impact of cost on treatment access, the effect on payers may be less severe than initially feared. A public health official stated that "if everyone had presented for care simultaneously and we had paid full price for those drugs, it would have broken the bank for Medicaid and even strained the ability of our HIV drug assistance program to keep up…neither one of those was a reality. *[Health official, State 5]*" Respondents described several factors that mitigated the impact of high drug costs on payers: the medical eligibility restrictions that payers used to limit treatment access were effective in doing so; newer medications have brought competition to the marketplace and thus lower prices; and some state governments have offered additional payments to insurance plans to motivate HCV treatment.

Treatment eligibility criteria changes by fee-for-service Medicaid do not necessarily apply to managed care

Even as fee for service Medicaid criteria have improved, respondents in four states discussed the continued variability in the practices of Medicaid managed care organizations. "The policy gets operationalized by…managed care plans…and they each operationalize the policy in their own way. Some…err on the side of approval and some err on the side of being very conservative and denying many requests. *[Treatment*

advocate]" While managed care is required to be as or more lenient than the state fee-for-service program, this requirement is not universally enforced: "it's very clear in the law that Medicaid managed care plans cannot use criteria that are more restrictive than the fee for service standard. Now, that doesn't always mean that all states follow that law…I think even where the state has been pretty clear with the managed care plans that they must follow the standard in fee-for-service or something more generous, the managed care plans to some extent do what they want to do and it's tough for the state to go around and enforce its standards against every managed care plan. *[Professional organization]*"

An official in another state was frustrated by the effect of this variability on providers: "I had my providers develop a spreadsheet looking at all the various plans…It was all over the place in terms of what the requirements were. That takes away from direct patient care. *[Health official, State 1]*" The complexity of the prior authorization process serves to discourage providers from offering HCV treatment and allows payers a way to "insert cogs into the machine *[Health official, State 2]*" For example, one plan "has things that seem like almost blatant obfuscation, like fax numbers where you send your prior auth and then they say they never received it. *[Treatment advocate]*" These processes, while not as explicit as eligibility restrictions described above, can "take hours on the phone…on hold…and filling out endless paperwork just to get the drug approved…It's a hidden cost of this work. I think those are being used even with open access, to restrict the flood, to dam up the demand a little bit and make it trickle a little bit more *[Health official, State 5]*."

Stigma, patient engagement, and provider availability are additional barriers to treatment access

Beyond cost and coverage policies, respondents in all states identified stigma around HCV and injection drug use as a second major barrier to HCV treatment access

that affected policymaking, providers, and patients alike. Stigma was “underlying everything we see, because while treatment is certainly very expensive, when you look at it compared to treatments for other big infectious diseases or big diseases in general, it’s not that much different. But I think because it’s a disease that predominantly impacts low-income people, people of color, people who are drug users, the perception is very, very different. *[Professional organization]*” Respondents with experience in HIV contrasted the strong political and advocacy movement surrounding HIV with the current environment in HCV, where affected populations have limited political voice. Stigma may also affect provider willingness to screen and treat HCV: “There are a lot of providers out there that don’t want to screen for hep-C because they think they’re going to bring in this flood of people who are drug users, and they don’t want to take care of those individuals. *[Health Official, State 1]*”

The third major perceived barrier to widespread HCV treatment access is patients’ and providers’ reluctance to initiate treatment due to a perceived lack of urgency and negative experiences with older treatments. Because HCV has a long asymptomatic latency period before affecting health outcomes, linking HCV patients to treatment is not perceived to be “as urgent as it feels with some other diseases, notably HIV. *[Health official, State 5]*” One respondent described “a little bit of a hangover from when the treatment regimens were more complicated, more toxic and less effective, so providers are a little bit slow to change their practice. *[Health official, State 5]*” Another described a similar effect for patients: “people with hepatitis C infections got such a negative image of hepatitis C treatment based on the pretty horrific experiences of the interferon treatments and their low efficacy that we didn’t see people banging down the doors at the very beginning. *[Health official, State 5]*”

Respondents in every state perceived a shortage of providers who were qualified to treat HCV, although this concern was highest in states with large rural HCV

populations. In two southern states, teaching hospitals were the most common places to receive HCV treatment, but these hospitals did not cover a wide geographic area. One public health official noticed "If you're not…where there're a lot of providers—and there's an awful lot of rural [areas]--you're not going to be travelling…to the doctor unless you're almost dead. *[Health official, State 4]*" In one Midwestern state, a large area "has really poor access to specialty care and very poor access to…medication therapy, substance use disorder, and even primary care is tough. *[Health official, State 6]*" States have responded to this in two ways: some states have attempted to lift requirements that the prescribing provider be a subspecialist, and some have invested in programs to encourage primary care providers to treat HCV. Respondents in 3 states mentioned programs that offered telephone or electronic consultation for HCV treatment, and officials in one other state were hoping to implement such a program.

An evolving political and fiscal environment can influence treatment access

The political and fiscal environment, both federally and within the states, can help to either facilitate or hinder treatment access. In one southern state, a health official observed that federal support for HCV is insufficient to finance HCV treatment through public programs, and supplemental state support is limited due to competing priorities. In another state, fiscal difficulties diminished public health funds, impairing not only direct treatment coverage, but also the ability to fund innovative programs and provider outreach initiatives. Respondents in two states specifically credited their state's political commitment to public health programs in aiding to promote HCV treatment access: "everyone in the administration recognized the importance of these drugs…[and that] the whole issue should be addressed equitably across all state payer sources. *[Health official, State 2]*"

A number of factors dynamically affect the politics surrounding HCV treatment that may have influenced the behavior of state Medicaid programs and insurance plans.

Media and advocacy groups have criticized restrictive policies. While federal support has been lacking in some veins, the Centers for Medicare and Medicaid services did issue guidance that criticized restrictions as well. Judicial decisions in several states have ruled against treatment restrictions, which has had the effect of motivating plans to improve treatment access: “states are getting to the point where they are worried that if somebody brings a lawsuit in the state, that they will have no choice but to make the change. So there are a few states that are trying to sort of get out ahead of that a little bit” [*Professional Organization*].

Finally, the 2016 U.S. Presidential election and potential changes to or repeal of the Affordable Care Act is an important factor. In contrast to a primarily optimistic outlook in interviews conducted before the election, respondents who were interviewed after the election expressed concern: “I think it’ll be a worsening medical situation for people who can’t meet a covered group in Medicaid. A larger monetary burden on the Department of Health to help to cover people that either were terminated from Medicaid, couldn’t get coverage through their employer plan, had no insurance…” [*Health Official, State 4]*. Another respondent felt that the recent improvements made by their state in terms of treatment access might be at risk: “We are an expansion state. If that were to change, that would limit access to a lot of people where we just finally made a couple baby steps in getting people able to be treated” [*Health Official, State 6].*

Individuals coinfected with HIV and HCV have additional mechanisms to facilitate HCV treatment

Although individuals coinfected with HIV/HCV are often more marginalized than HCV monoinfected individuals, they have better access to HCV treatment as a result of government programs for HIV care. AIDS Drug Assistance Programs (ADAPs) can facilitate treatment access by providing direct medication coverage for HIV and related conditions, purchasing insurance for enrollees, and paying copays and coinsurance. In

states without the Medicaid expansion, ADAP may cover HCV treatment for coinfected individuals who are not eligible for Medicaid, as income requirements for enrolling in ADAP are generally more lenient than they are for Medicaid. In every state we studied, ADAP's requirements for approval of HCV medications were minimal compared to requirements of Medicaid programs, though this may not be representative of all state ADAP programs. As programs that primarily provide treatment coverage, ADAPs are generally "not able to cover…cost of lab testing and medical visits, *[professional organization]*" though some programs have launched initiatives to do so. While most states called ADAP a "payer of last resort," allowing individuals to receive HCV therapy from ADAP if that therapy was denied through their primary insurance plan, one state program did not provide "gap coverage on a drug by drug basis. *[Health official, state 5]*" This variation can serve as a source of provider confusion which slows uptake: even in states where ADAPs covered HCV treatment, respondents indicated that providers were not always aware that ADAP programs could be used in this way. In addition to ADAP, HIV program infrastructure can provide additional services such as housing support, care coordination, and specially funded centers and health homes: these mechanisms can be used to either promote HCV treatment access directly, or to provide funding for innovative programs.

Discussion:

We interviewed experts in the HCV treatment landscape in the United States both nationally and within six states with diverse characteristics to understand barriers to DAA uptake and promising policy strategies. Our findings show that the cost of HCV therapy limits access by motivating payers to impose medical eligibility criteria and prior authorization requirements for treatment, in turn discouraging providers from offering treatment and patients from seeking it. The effects of costs on payers have been blunted by access limitations, and discounted prices due to negotiation and competition.

This, in addition to legal and political pressure to provide treatment, has motivated fee-for-service Medicaid programs to lighten eligibility criteria. However, managed care organizations can have a diverse set of authorization requirements even within the same state which can frustrate state officials and further discourage providers from offering treatment. Further, ADAP programs allow for additional coverage options for HIV/HCV coinfected individuals that are not available to HCV monoinfected. Beyond insurance coverage, other barriers to treatment access include stigma, patient and provider reluctance around treatment. Regional variation in access to providers and in political support and funding for HCV services limit the take-up in some regions.

Our findings detail the mechanisms by which pricing hinders access: most significantly by driving payers to limit treatment access, but also by downstream administrative barriers such as prior authorization paperwork, which discourages providers from offering treatment. These findings are consistent with studies of prior authorizations and denials for HCV DAA, which find rates of denials up to 29% and long wait times before authorization decisions.[33, 34] Treatment eligibility criteria, which have drawn criticism for being overly restrictive,[35, 36] are improving for the fee-for-service Medicaid programs in the states that we studied. This improvement is consistent with findings from a report by the National Viral Hepatitis Roundtable in 2016, which found that compared to the findings in 2014, 14 fee-for-service Medicaid programs had improved their access criteria with regards to disease severity, 6 with regards to sobriety, and 8 with regards to provider specialty.[30] Findings from our study indicate that these changes are primarily related to lower-than-expected demand, increased market competition, and political and legal pressures. While the 2016 report did also find that MCOs might have criteria more restrictive than that of the state program, our respondents stressed the variability between different MCOs and the lack of

transparency in their practices as significant barriers to understanding the coverage landscape.

Respondents indicated regional variation between and within states based on geography, economy, and political climate. Access to treating providers in rural areas was seen as a challenge even in states where access was not strongly limited by insurance requirements. A 2012 study in Wisconsin showed that of 72 counties, 51 had no infectious diseases or gastroenterology providers, potentially limiting HCV treatment.[37] Research in other, related disease states also supports this finding: rural Americans may have poorer access to substance use treatment,[38] HIV treatment,[39]and preventive care services[40] than those in urban areas. This finding is especially relevant for HCV given the ongoing rural epidemic related to injection drug use.[5, 6] Efforts to address this, including using telemedicine to augment access to specialty consultation can be successful, but require a public commitment to public health infrastructure in order to be implemented.[41] If new federal initiatives reduce or restructure funding to Medicaid programs, the burden on state budgets may increase, and other patient populations may be prioritized for limited resources.

In all states, individuals co-infected with HIV/HCV have better access to DAA treatments than mono-infected individuals and many of our respondents have experience working in the field of HIV. While some have called for a response to HCV that mimics ADAPs for HIV, this is unlikely to be forthcoming in the current political climate.[42] Despite this, states can leverage a robust HIV treatment infrastructure in order to promote policies that focus on HCV treatment by utilizing existing links between public health officials and providers. For examples, epidemiologic surveillance strategies used for HIV, such as the cascade of care model, has been applied to HCV.[43-45] Coordinated care delivery models that are effective in HIV can also be applied

to patients with HCV, such as patient navigation to improve linkage to care,[46-48] and integration of primary care providers to improve treatment capacity.[49-52]

Our study has a number of limitations. We selected diverse states based on their geography, features of their health systems, and HCV treatment policies to solicit a range of perspectives, but with a qualitative sampling design the findings should not be interpreted as the average response. Within each state, we recruited primarily individuals whose jobs were focused on treatment access, and who were inclined to promote treatment access in their own jurisdictions. Further research with individuals whose jobs involve allocating state resources may reveal different results. Our respondents' own uncertainties about price negotiations suggests that further work is needed to explore the true costs of HCV therapy to different payers. We attempted to minimize bias in data interpretation by having two investigators independently code interview transcripts and ongoing project meetings to discuss the codebook and results. Finally, some of our interviews took place before the 2016 U.S. presidential election, and others after. Proposed changes in federal health policy surrounding the change in administration may have affected the views of study respondents differently before versus after the election.

Eliminating the HCV epidemic will take a concerted effort from public health and healthcare infrastructure. While overcoming the price barrier is necessary, our findings show that it is not sufficient. Growing the provider workforce in high need areas and resolving urban-rural disparities in access to care will be important steps for treatment scale up. The stigma surrounding HCV and substance use is a barrier to informed policy and care that must be addressed at the level of patients, providers, health systems, and governments. Finally, all of this must be built on a bedrock of healthcare access, a continued challenge in today's U.S. policy environment. The committed, multi-level response to the HIV epidemic that has evolved over the past thirty years can serve as

an example for the response to HCV. While our study detailed many challenges, it was clear that the therapeutic innovations of the past few years have given us an opportunity to halt an epidemic that is poised to affect millions.

APPENDIX

Interview guide:

Introductory questions:

First, I would like to ask you some general questions about your position and your experience with this issue.

1. What is your current position within your program/organization?
2. How long have you been involved with this program/organization?
3. Can you describe your role in the context of hepatitis C treatment access and utilization?

Mechanisms for HCV DAA acquisition in your state or region

As you know, new medications for the treatment of hepatitis C are becoming available. These medications are very effective, but they can be difficult for some patients to obtain because of expense. I would like to explore your experience with this issue.

4. What are the mechanisms that patients in [state/region] have available for accessing treatment to hepatitis C?
   - **a.** Specifically patients on Medicaid, if not mentioned
   - **b.** Any planned or innovative programs at the state or local level?
   - **c.** Any specific differences by subpopulation: for instance HIV infected or injection drug users

5. Can you discuss any recent or planned policy changes regarding providing access to HCV medications for patients enrolled in Medicaid? In other insurance programs?
   - **a.** What are the factors that led to these policies being implemented?
   - **b.** What were the barriers to putting these policies in to place?

6. Have there been any discussion or action regarding adding new HCV medications to public insurance formularies (Medicaid, ADAP if applicable)? If so, can you describe?

Barriers to DAA acquisition in your state or region

7. What are the biggest barriers that patients in [state/region] face for accessing HCV treatment?
   a. Specifically for patients on Medicaid, if not mentioned

b. Specifically re: drug pricing, provider availability, insurance status if not mentioned

8. Many insurance plans have specific authorization requirements that patients must meet before obtaining HCV treatment (example: fibrosis status, substance use abstinence, provider specialty, HIV viral load suppression, treatment readiness). Can you describe how these authorization requirements affect treatment access in [state/region]?
   a. Ask about specific requirements if not mentioned
   b. Any recent changes or plans to change, and if so, what motivated the changes?
   c. Are requirements consistent across insurance plans? (Medicaid vs managed Medicaid vs commercial, Medicare, etc)

9. How would you describe HCV treatment uptake or utilization in [state/region], aside from medication access? What are the other barriers to treatment uptake?

Contrast of the HCV/HIV coinfected population to HCV monoinfected population

10. Can you discuss any differences in obtaining HCV treatment for the HIV coinfected population compared to the HCV monoinfected population?
    a. If not mentioned, ask specifically about ADAP programs, treatment eligbility criteria, provider availability

Additional factors (if not already covered) and future vision

11. Does your program interact with consumer or patient advocacy groups? What role, if any, has advocacy played in HCV treatment access in [state/region]?

12. What role, if any, have recent lawsuits and judicial decisions played in HCV treatment access in [state/region]?

13. What role, if any, has federal government and professional society guidance played in HCV treatment access in [state/region]?

14. What are your expectations regarding how state programs in general, and yours in particular, will respond in the future to the challenge of providing HCV treatment access?

Closing

Do you have any other comments on the topics that we discussed?

Is there anyone else that you think we should talk to about the issue of obtaining hepatitis C medications for HIV infected patients?

It's possible that as I continue to interview people, new questions might come up. Is it okay if I get back to you, via email, if any new questions do arise?

List of Codes

Factors:

Administrative barriers–*Code prior authorizations, lengthy approval process, other non-financial non-medical barriers to treatment.*

Advocacy Work – *code referring to community advocates, lobbying, etc.*

Cost of treatment – *Code related to drug cost (for patients, insurers, govt, etc), drug pricing mechanisms, coupons, rebates, etc*

Disease Exceptionalism – *Code refers to special policy/political/financial attention given to a specific disease, e.g. HIV infected.*

Guidelines - *referring to AASLD/IDSA treatment guidelines*

Innovative solutions – *use when a respondent mentions an idea or solution that they have heard of, e.g. rebates, carve-outs, centers of excellence, health homes, provider training, etc*

Legal Factors - *Code at mention of any of the lawsuits or legal challenges to treatment restrictions*

Medical Eligibility Criteria

> Fibrosis – *Code fibrosis stage or general "disease severity" criteria*
>
> Treatment specialty – *Code need for specific specialty to give treatment, also difficulty accessing said specialties.*
>
> Abstinence – *Code need for substance use abstinence including provider documentation, treatment engagement, and urine toxicology testing*
>
> HIV treatment/ suppression – *Code need for HIV treatment or viral load suppression for HIV/HCV coinfected patients*
>
> Treatment Readiness – *Code general references to "treatment readiness" or concerns about ensuring adherence before starting treatment*

Patient Assistance Programs – *Code pharma company funded assistance programs*

Policy Creation Process -- *code if someone is describing the process for policy changes*

Political Environment – *code when someone is talking about political motivation for changes, or political reluctance for change*

Stigma – *code when someone mentions stigma by name or discrimination vis a vis HCV infected populations*

Transparency – *Code refer to transparency by name, or general difficulty accessing information from gov't, insurance, or drug companies that is perceived to be important/necessary information by the participant*

Treatment Uptake – *Code when subject refers to treatment uptake*

Factors, NOS – *Other factors, passages, or themes that may be interesting but not specified above*

Stakeholders, their motivations and their interactions:

Public Insurance – *code at Medicare, Medicaid, ADAP*

Private insurance- *code at mention of commercial insurance*

Government – *code at federal or state government response, policies, guidance, etc*

Healthcare system / infrastructure – *code related to health systems – e.g. HIV program infrastructure, substance use treatment programs, academic medical centers, etc*

Patients – *Code related to patients or patient subgroups. Child code for HIV infected*

HIV Coinfected – *Code related to HIV/HCV coinfected patients*

Media – *code related to media pressure*

Pharmaceutical Companies

Cooperation between stakeholders - *code when someone talks about negotiations, communication, or cooperative tactics between players*

Conflict between stakeholders – *code when someone talks about negative interactions between stakeholders*

Stakeholders, NOS – *new major actors or stakeholders that are mentioned but are not listed above*

Miscellaneous:

Participant Introductions – *Code the response to the "Who are you and what do you do" question*

Future predictions – *include speculation about the future, hopes, fears, planned interventions*

Interesting Quotes

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